Remarks

Upon entry of the foregoing amendments, claims 14-16 and 18 are pending. Claim 17 is hereby cancelled without prejudice thereto or disclaimer thereof the subject matter contained therein. Claim 16 is sought to be amended without prejudice thereto or disclaimer thereof any subject matter omitted. Applicants believe that no new matter is introduced by these claim amendments, and their entry is respectfully requested.

I. Claim Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 16 and 17 are rejected under 35 U.S.C. §112, first paragraph, for allegedly "failing to comply with the enablement requirement." Office Action, page 2. For reasons previously provided in Applicants' Response to Office Action filed via facsimile on October 23, 2006 and wholly incorporated here, Applicants respectfully disagree with the Examiner. Solely to expedite prosecution and not in acquiescence to the rejection, however, Applicants have amended claim 16 and cancelled claim 17. Accordingly, this rejection is now believed to be moot. Applicants request that the Examiner reconsider and withdraw the rejection.

II. Claim Rejections Under 35 U.S.C. §103(a)

Claims 14-18 are rejected under 35 U.S.C. § 103(a) for allegedly being unpatentable over European Patent Application 0712926 A2 (herein, "the '926 application") in view of Schlesinger *et al.* "Togaviridae: The Viruses and Their Replication," Fields Virology, 3d ed., Ch. 27, pp. 825-827, Bernard N. Fields *et al.* eds., Lipincott-Raven Publishers, Philadelphia (1996) (hereafter, "Schlesinger *et al.*"). Applicants respectfully disagree with the rejection.

A. Publications Used to Reject Composition Claims Under 35 U.S.C. §103 Must Enable the Skilled Artisan to Make the Claimed Compositions

After the U.S. Supreme Court decided Graham v. John Deere, 383 U.S. 1, 148 USPQ 459 (1966), the USPTO policy regarding questions of obviousness focused on four factual inquires. M.P.E.P. § 2141(I) (2006). Among other inquires, the scope and contents of the prior art must be considered. *Id.* The M.P.E.P. refers to sections 2121-

2129 for guidance in determining whether the substantive content of the applied publications support a rejection under 35 U.S.C. § 103. *See id.* at §2141.01 (II). Section 2121.01 states that a reference must include an enabling disclosure in order to be applied in a rejection:

> "In determining that quantum of prior art disclosure which is necessary to declare an applicant's invention 'not novel' or 'anticipated' within section 102, the stated test is whether a reference contains an 'enabling disclosure'... ." *In re Hoeksema,* 399 F.2d 269, 158 USPQ 596 (CCPA 1968). The disclosure in an assertedly anticipating reference must provide an enabling disclosure of the desired subject matter; mere naming or description of the subject matter is insufficient, if it cannot be produced without undue experimentation. *Elan Pharm., Inc. v. **>Mayo Found. For Med. Educ. & Research<*, 346 F.3d 1051, 1054, 68 USPQ2d 1373, 1376 (Fed. Cir. 2003) (At issue was whether a prior art reference enabled one of ordinary skill in the art to produce Elan's claimed transgenic mouse without undue experimentation. Without a disclosure enabling one skilled in the art to produce a transgenic mouse without undue experimentation, the reference would not be applicable as prior art.). A reference contains an "enabling disclosure" if the public was in possession of the claimed invention before the date of invention. "Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his [or her] own knowledge to make the claimed invention." *In re Donohue*, 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985).

In section 2121.02, the M.P.E.P. also relates this legal requirement to composition claims:

> Where a process for making the compound is not developed until after the date of invention, the mere naming of a compound in a reference, without more, cannot constitute a description of the compound. *In re Hoeksema*, 399 F.2d 269, 158 USPQ 596 (CCPA 1968).

Hence, in order for publications to properly be used in support of a rejection of composition claims under 35 U.S.C. § 103, the publications must enable the skilled artisan to make the claimed compositions. For reasons discussed below, the publications cited by the Examiner fail to enable the skilled artisan to make the claimed compositions.

B. The '926 Application and Schlesinger et al. Alone or Combined do not Enable the Skilled Artisan to Make the Claimed Compositions

i. The Publications Fall Short of Identifying FPDV as a Member of the Togavirus Family, and Consequently, they Fail to Enable the Skilled Artisan to make the Claimed E2 Protein

Nothing in the '926 application or in Schlesinger *et al.* alone or in combination would enable the skilled artisan to make the claimed recombinant E2 protein of fish pancreatic disease virus (FPDV). For reasons explained in greater detail below, the '926 application does not itself explain that the FPDV described therein is in fact a Togavirus. Even if it were presumed to be a togavirus, there are a variety of genuses within the Togavirus family, and a substantial lack of homology and lack of conserved domains even within the various genuses that the skilled artisan would not be able to make the claimed protein.

Applicants stress to the Examiner that the '926 application does not state that the FPDV described therein is a Togavirus. Rather, the '926 application merely states that "FPDV is a *toga-like* virus." Page 2, line 48, emphasis added. This statement falls far short of definitively classifying it as a member of the Togavirus family. The applicants in the '926 application merely examined the FPDV by electron microscope and noted that it had morphological similarities to species within the Togavirus family. Page 2, lines 42-43. As late as 1999, FPDV had still not been definitively identified as a member of the Togavirus family. Marian F. McLoughlin, an inventor on the '926 application, co-authored a publication stating that "[o]n the basis of physicochemical characteristic and structural morphology, . . . [fish pancreatic disease virus] was tentatively classified as a 'toga-like' virus." *See* page 188, left column of Weston *et al., Virology 256*: 188-195 (1999), provided herewith as Exhibit A. Hence, the skilled artisan upon reading the '926 application would understand that FPDV has physical characteristics similar to members of the Togavirus family, but would not assume that it was in fact a member of the Togavirus family.

Moreover, nothing in Schlesinger *et al.* would lead the skilled artisan to believe that the FPDV described in the '926 application belonged to the Togavirus family. Schlesinger *et al.* states that members of the Togavirus family "were all grouped together

on the basis of size, on their having a single-strand nonsegmented RNA genome that functions as a messenger RNA, and on the ability of many of the members to replicate in and be transmitted by mosquitos." Page 825, left column. The '926 application does not describe FPDV as having all these properties. Hence, the skilled artisan would have little reason to assume that it was definitively a member of the Togavirus family.

Moreover, the skilled artisan would appreciate the tenuousness of labeling FPDV as belonging to the Togavirus family solely on the basis of morphology observed with the electron microscope. Indeed, the *second edition* of Fields Virology indicates that the Togavirus family includes the Alphavirus genus, the Rubivirus genus, the Pestivirus genus and the Arterivirus genus. *See* Exhibit B, page 703. Schlesinger *et al.* was published in the third edition of Fields Virology, which confirms that the Togavirus "family was originally much larger . . . ." Schlesinger *et al.*, page 825, left column. Hence, viruses once grouped together on the basis of morphology were later determined to belong to wholly different families. Moreover, the skilled artisan would not expect extensive genetic similarities solely on the basis of morphological similarities observed through an electron microscope, and thus would not have reason to believe that FPDV contained an E2 protein. Hence, the publications relied upon in the 35 U.S.C. § 103 rejection do not enable the skilled artisan to make the claimed protein.

If neither the '926 application or Schlesinger *et al.* alone or in combination identified FPDV as a member of the Togavirus family, the skilled artisan would have no reason to believe or expect that FPDV contained the claimed E2 protein. Hence, these publications do not enable the skilled artisan to make the claimed E2 protein. Consequently, these publications alone or combined fail to set forth a proper rejection under 35 U.S.C. § 103(a).

ii. Even if the Publications Sufficiently Led the Skilled Artisan to Believe that FPDV is a Member of the Togavirus Family, a Substantial Lack of Sequence Homology Between FPDV and Other Members of the Togavirus Family Would Prevent the Skilled Artisan from Making the Claimed E2 Protein Without Undue Experimentation

Notwithstanding the arguments made above in section ***II.B.i.***, Applicants respectfully assert that the lack of sequence homology between and amongst FPDV and known members of the Togavirus family prevents the skilled artisan from making the claimed E2 protein without undue experimentation. Moreover, the '926 application and Schlesinger *et al.* do not provide any information regarding the FPDV E2 protein. Hence, these publications do not enable the skilled artisan to make the claimed protein, and do not properly set forth a rejection under 35 U.S.C. § 103.

According to Schlesinger *et al.*, Rubiviruses and Alphaviruses both belong to the Togavirus family. *See* page 825, left column. However, there is no homology between Rubiviral and Alphaviral genomes:

> . . . the rubella genome and consequently the viral proteins proved to be distinct from those of alphaviruses. The cDNA sequence of the rubella subgenomic mRNA shows an unusually high G/C content. The derived structural protein sequences have no sequence homology to alphavirus proteins, although the gene order of 5' capsid-E2-E1 is identical to that of the alphaviruses.

See Exhibit B, page 704, right column, last paragraph (citations omitted). Applicants note that this excerpt comes from the *second edition* of Fields Virology. Hence, the skilled artisan upon reading Schlesinger *et al.* would be aware that there is no genomic or protein sequence homology between rubiviruses and alphaviruses. Moreover, post-translational processing of rubiviral proteins differs from that of alphaviral proteins. Exhibit B, sentence bridging pages 704-705. Hence, even if it was presumed that FPDV belonged to the Togavirus family, such information is insufficient to allow the skilled artisan to identify and make the claimed E2 protein.

Moreover, sequence comparisons show that there is very little homology between FPDV and known alphaviruses. For example, "[t]he percentage of amino acid sequence identity was determined using pairwise comparisons between the structural region of

SPDV and that of other alphaviruses and was shown to be uniform, with percentage identities falling between 32 and 33% (Table 2)." Exhibit A, page 189, left column at bottom, and Table 2. *See also* Table 4 of Exhibit C (Powers, A.M. *et al., J. Virol. 75*(21): 10118-10131 (2001)). This lack of homology is not surprising considering that in contrast to FPDV (isolated from fish), all the Togaviruses discussed prior to the captioned invention were not isolated from cold-blooded host animals. Indeed, this explains why phylogenetic trees show FPDV to be only distantly related to other alphaviruses. *See* Exhibit C, figures 2 and 3 on pages 10126 and 10127. The authors of Exhibit C also point out that "SDV and SPDV . . . appear to represent a distinct complex based on their sequence divergence. They clearly occupy dramatically different niches and genetic lineages from all remaining alpahviruses, indicating that they are not variants of an established species." *See* page 10129, last sentence of left column to first sentence of right column.

Moreover, the structural protein E2 has a major antigenic region that is conserved in most alphaviruses. *See* Exhibit A, page 189, right column, second full paragraph. In this region, however, the FPDV E2 protein only contains three invariant residues. *See id.* Hence, absent Applicants' specification, it would require undue experimentation for the skilled artisan to obtain the claimed protein.

Taken together, these facts indicate that if there would have been a common ancestor at all, the divergence between the aquatic Toga-like virus and the terrestrial Togaviruses must have occurred in the very distant past. Hence, the skilled artisan would not expect any shared characteristics of signifcance between the terrestrial Togaviruses and FPDV.

In order to make the claimed FPDV E2 proteins without undue experimentation, the skilled artisan must have a starting point from which the genome can be sequenced and from which genes can be identified. The publications cited by the Examiner in the § 103 rejection do not provide such a starting point, and do not enable the skilled artisan to make the claimed proteins. Moreover, other publications (provided in accompanying Exhibits) demonstrate that there is a dramatically low sequence identity between FPDV and other alphaviruses, making it require undue experimentation to design proper primers with which the claimed protein can be cloned. Furthermore, FPDV E2 does not appear to

contain other alphaviral conserved regions or motifs. Hence, the skilled artisan (absent Applicants' specification) would not have been able to make the claimed proteins.

In summary, neither the '926 application or Schlesinger *et al.* provide the skilled artisan with any sequence information to isolate and obtain the claimed FPDV E2 protein. Moreover, the state of the art at the time of Applicants' invention indicates that the various genuses within the Togavirus family are genetically distinct and not homologous. Moreover, the different species within the alphavirus genus have very low homology relative to one another. Hence, in the absence of Applicants' specification, the skilled artisan would have an undue burden in making the claimed FPDV E2 protein. Accordingly, the publications forming the basis of the Examiner's rejection under 35 U.S.C. § 103 do not enable the skilled artisan to make the claimed proteins, and thus do not form a proper basis for the rejection.

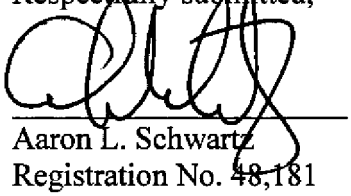
For all of the aforementioned reasons, Applicants kindly request that the Examiner reconsider and withdraw the rejection.

Conclusion

Applicants do not believe that any other fee is due in connection with this filing. If, however, Applicants do owe any such fee(s), the Commissioner is hereby authorized to charge the fee(s) to Deposit Account No. 02-2334. In addition, if there is ever any other fee deficiency or overpayment under 37 C.F.R. §1.16 or 1.17 in connection with this patent application, the Commissioner is hereby authorized to charge such deficiency or overpayment to Deposit Account No. 02-2334.

Applicants submit that this application is in condition for allowance, and request that it be allowed. The Examiner is requested to call the Undersigned if any issues arise that can be addressed over the phone to expedite examination of this application.

Respectfully submitted,



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